

Foerster (Fr.)

Comparative  
Microscopical Studies of the  
Ovary

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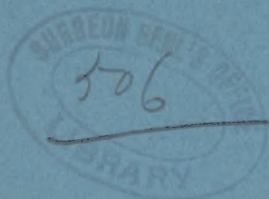
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## COMPARATIVE MICROSCOPICAL STUDIES OF THE OVARY.

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### THE CORPUS LUTEUM OF PREGNANCY.

EVERYBODY is familiar with the time-honored expression, "corpus luteum." It is in a certain sense a misnomer, as we use the same term for the outcome of menstruation as well as for the outcome of pregnancy, affixing the explanatory epithet *verum* or *spurium*.

I am convinced that under normal conditions a corpus luteum menstruationis, or spurium, as usually described, does not exist, that whenever such a growth appears we invariably find it in a pathological ovary.

In a previous article <sup>1</sup> I described the so-called corpus luteum spurium, assenting in general to the researches of Dr. M. D. Jones. At present I propose to establish a distinction between the pathological endothelioma—so-called corpus luteum spurium—and the physiological corpus luteum.

Endothelioma is a growth in the ovary resembling the corpus luteum of pregnancy, but, in contradistinction to the latter, it is persistent, productive of pain, and liable to undergo changes, of which the formation of hematoma is the most important. Both formations are the result of ovulation: the corpus luteum of pregnancy developing in the normal ovary congested by supervening pregnancy; the endothelioma, on the contrary, in a pathologically altered ovary. In the former we see this body return to ovarian structure with the lessened congestion after delivery, while in the latter the growth, under the continuous irritation of oöphoritis, persists, nay, increases, to become a lasting source of bodily ailment.

The study of the corpus luteum verum, its development, evolution, and involution, is the topic of my present paper.

I thought it best to first resort to the examination of ovaries

<sup>1</sup> AMERICAN JOURNAL OF OBSTETRICS, vol. xxv., No. 5.

of domestic animals, since it appears reasonable to assume that such animals delivered to the abattoir may safely be considered to have been in normal condition. I have selected the sow, ewe, and cow, informing myself either as to the time elapsed since last delivery, or knowing exactly, by inspection of the contents of the uteri, how far gestation had progressed. I have entered also the study of a human corpus luteum from a case where I had performed laparotomy for tubal pregnancy of the left side, where I found a corpus luteum in the corresponding ovary. The certainty of diagnosis, as proven by anatomical examination of the removed organs, has induced me to select this case for microscopical studies.

The literature of the corpus luteum up to recent date is given in an introductory to an excellent article by Benekiser.<sup>1</sup> This author confined himself to the microscopical study of the corpus luteum of the sow. The conclusions he arrives at I would not consider altogether satisfactory, since he does not attempt to define the tissues composing this formation.

Whenever a matured Graafian follicle bursts, a loss of substance is the result after the escape of the ovum. The cavity thus formed must be filled up in a way similar to the filling of a cyst artificially emptied and treated by the surgeon with some irritating agent, or a loss of substance healing under aseptic conditions. The process of healing in the former instances is pathological, in the latter physiological; but in both cases the process in its intimate features is identical. Additional to the healing of a burst ovarian follicle is the feature of a more or less intense hemorrhage, since it is a blood clot that fills the cavity immediately after rupture. Should pregnancy follow the bursting of the Graafian follicle, obviously the hyperemia thus established in the female genital organs will cause a more intense reaction in the walls of the emptied follicle as well as in the vicinity. The final result is known to be a nodule of considerable size, far in excess of the original loss of substance. The results of my researches enable me to furnish a definition of the newly formed tissue as compared with analogous formations in other parts of the body.

The method applied for the preparation of the microscopical specimens is that advised by C. Heitzmann, in whose laboratory my studies were carried on—viz., hardening of the fresh ovary,

<sup>1</sup> Archiv für Gynäkologie, xlii.

or an ovary preserved in alcohol, in a one-half of one per cent solution of chromic acid, staining of the sections with ammoniacal carmine, and mounting in chemically pure glycerin.

Doubts have been raised against the feasibility of this method. They have induced me to examine specimens preserved and hardened in alcohol, stained with various agents, and mounted in Canada balsam. From my own experience I can vouch for the superiority of the method above mentioned, which yielded the clearest images, best fit for the study even with the highest

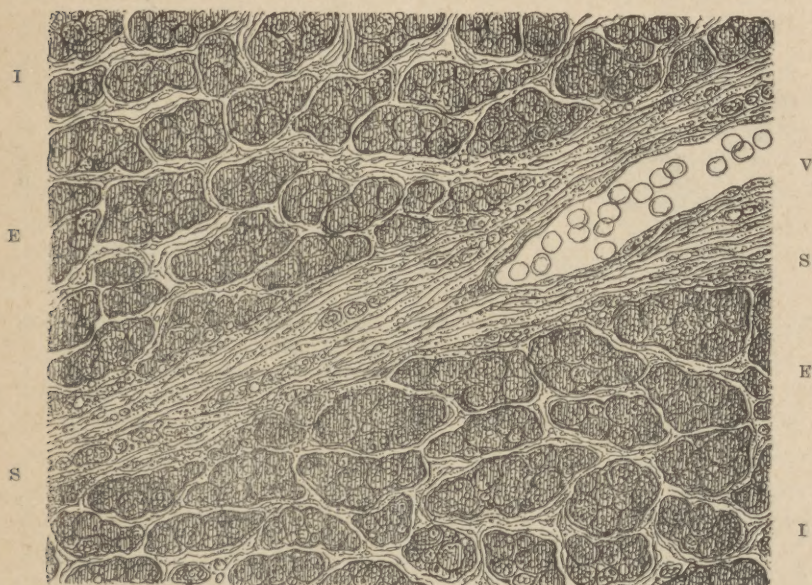


FIG. 1.—Corpus luteum in tubal pregnancy of two months; lobular portion.  $\times 400$ . V, vein holding red blood corpuscles; S, S, septum of delicate fibrous connective tissue between two lobules; E, E, endothelia composed of medullary corpuscles; I, I, delicate interstitial connective tissue.

powers of the microscope. Zeiss apochromatic objectives and compensating oculars were used.

*A. The Human Corpus Luteum of Two Months' Standing.*—The nodule, the size of a cherry pit, is embedded in the cortex of the ovary, and separated from the surface by a thin layer of cortical tissue. It consists of two portions: a peripheral, distinctly lobulated; and a central one, non-lobulated, holding in its interior a fresh clot of blood, probably formed shortly before extirpation. In the clot a separation has taken place of

the fibrin from the red blood corpuscles, which latter have a fresh, unchanged appearance and are saturated with hemoglobin. The lobular appearance of the peripheral portion is caused by radiating septa of fibrous connective tissue in connection with the outer capsule as well as with the central tissue of the nodule.

The outer capsule is made up of fibrous connective tissue, freely supplied with blood vessels, arteries, veins, and capillaries. The arteries and veins—the latter being filled with blood—

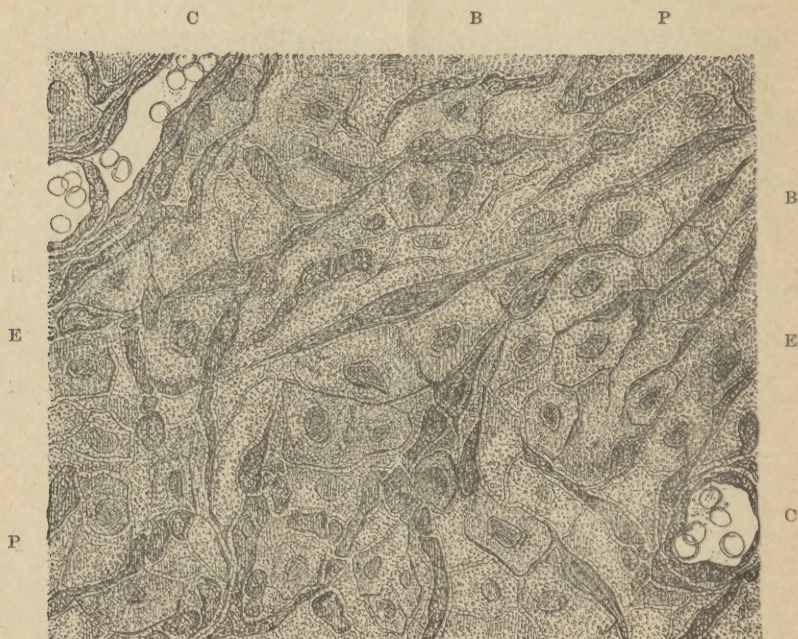


FIG. 2.—Corpus luteum in tubal pregnancy of two months; central portion.  $\times 400$ . P, P, protoplasmic bodies, partly branching and interconnecting; E, E, nucleated endothelia in the process of transformation to basis substance; B, B, basis substance, still exhibiting the structure of protoplasm; C, C, capillary blood vessels in longitudinal and transverse sections.

are far more numerous than in the normal cortex of the ovary, including the cortex of that under consideration. The septa radiatingly traversing the nodule carry a large number of blood vessels, especially arterioles, in contradistinction to the central portion, in which blood vessels are scanty and mainly of the venous and capillary type. Since the whole nodule is newly formed, it is reasonable to maintain that all blood vessels of the

capsule, the septa, and the central portion likewise are newly formed. The tissue within the lobules is scantily supplied with blood vessels, and these are almost exclusively of the capillary type. With medium powers of the microscope this tissue has the appearance presented in Fig. 1.

We see groups or clusters of embryonal or medullary corpuscles embedded in an extremely delicate fibrous connective tissue carrying small capillaries. The medullary corpuscles are of a light-brown tint, though distinctly stained by a solution of ammoniacal carmine. In such stained specimens the septa have assumed a pure pink, the clusters, on the contrary, a brownish-pink color. The medullary corpuscles are of greatly varying sizes, coarsely granular, without nuclei, and separated from one another by a delicate light layer of cement substance. Their connections are rather feeble, and in some places of the specimen they appear torn asunder, leaving artificial gaps. High powers of the microscope demonstrate a direct connection of the embryonal corpuscles by means of delicate threads, the same as in the indifferent corpuscles, building up the embryo after the segmentation has passed, or in the extremities spouting out from the embryo in the third or fourth week of embryonal life.

The septa are composed of fibrous connective tissue, the same as the capsule, and abundantly supplied with protoplasmic bodies, but the less infiltrated with basis substance the nearer the central portion of the corpus luteum. Quite different is the aspect of the central portion (see Fig. 2).

Here we observe numerous partly branching and interconnecting protoplasmic bodies of greatly varying shapes, well stained with ammoniacal carmine, whereas the portions between the bodies are only of a pale-pink color or lack color altogether. With medium powers of the microscope many of the branching protoplasmic bodies appear nucleated and all of them coarsely granular. In the tissue between them, on the contrary, the nuclei are scattered, globular, and the intervening fields finely granular. On analyzing the latter fields we can easily see the division into finely granular bodies or fields, greatly varying in size. In this portion we obviously have a transition of protoplasm into basis substance. Through this transformation the protoplasm is paling, since it is infiltrated with basis substance, whereby the original reticulated structure is retained and still

perceptible. The nuclei of the protoplasmic bodies at first remain unaltered and tingible with carmine; later on many of the nuclei are likewise infiltrated with basis substance, becoming pale and faintly discernible, until at last the majority of nuclei are rendered invisible by being saturated with basis substance, the same as the rest of the protoplasm.

The features described in the human corpus luteum are worth studying with the highest powers of the microscope (Fig. 3).

The lobular portion (E) is seen to be composed of clusters of

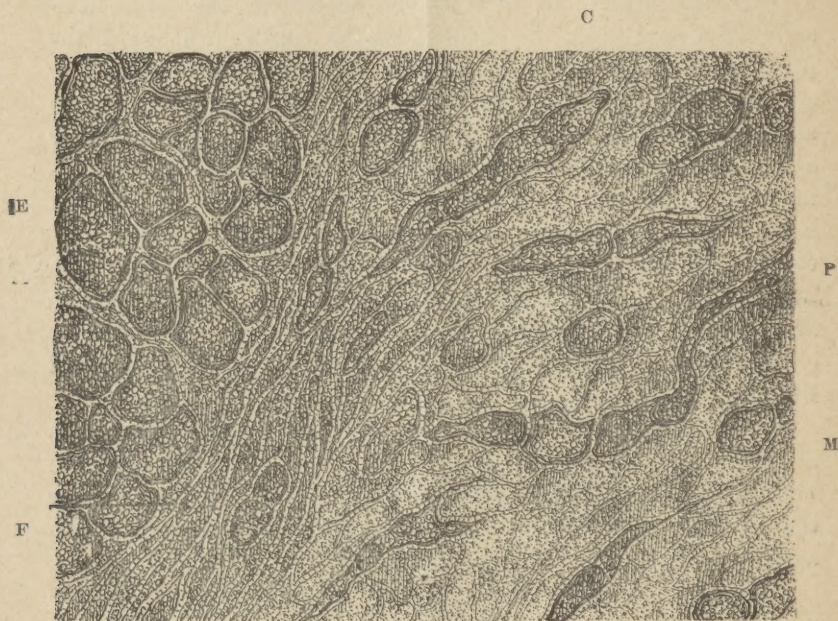


FIG. 3.—Corpus luteum in tubal pregnancy of two months.  $\times 1200$ . E, endothelia of the lobular portion, made up of medullary corpuscles; F, fibrous connective tissue forming septa between the lobules and the central portion of the corpus luteum; C, central portion of corpus luteum; P, protoplasmic bodies of central portion; M, protoplasm in transformation to myxomatous basis substance.

indifferent or medullary corpuscles. This fact is of importance, since it enables us to understand the structure of the fully developed corpus luteum. The large protoplasmic bodies appearing in the corpus luteum, termed by previous authors "lutein cells" or "epithelioid cells," I shall term endothelia. The study of the early stage of its development entitles me to the assertion that each endothelium is the result of the confluence of a number of indifferent or embryonal corpuscles. A certain number (eight

to twelve), originally coarsely granular, non-nucleated, and separated from one another by light rims of cement substance, though interconnected by extremely delicate fibres, coalesce to form a large protoplasmic body, termed endothelium, which contains, as a rule, one distinct nucleus.

The lobules of the peripheral portion are surrounded by fibrous connective tissue. This tissue sends tender offshoots between the groups of embryonal corpuscles, which remain even at the full height of the development of the corpus luteum, ensheathing each endothelium.

In our specimen the fibrous tissue of the septa shows complete infiltration with glue-yielding basis substance, and holds a limited number of protoplasmic bodies, so-called connective-tissue corpuscles. Upon approaching the central portion the fibrous connective tissue is seen to be more protoplasmic in nature and more freely supplied with connective-tissue corpuscles. The portion of the septa ensheathing the single lobules (Fig. 3, F) is but sparingly infiltrated with basis substance and exhibits the features of an early stage of development. This layer blends with the tissue of the central portion (Fig. 3, E). Here the elongated protoplasmic bodies are coarsely granular, indistinctly nucleated, whereas the fields of the basis substance still admit the recognition of the reticulated structure of the protoplasm and its composition by a number of bodies, greatly varying in size and shape. The central portion bears all the characteristic features of a myxomatous tissue, resembling that of the umbilical cord, although the connections of the elongated protoplasmic bodies are by no means as marked in the corpus luteum as they are in the tissue of the umbilical cord.

Based upon these researches, I maintain that the peripheral or lobular portion of the human corpus luteum of two months is made up of embryonal or indifferent tissue. The central portion is further advanced in development to the formation of a myxomatous tissue. We have, therefore, a granulation tissue before us, as we see in the granuloma in the process of healing of a wound after loss of substance. The earliest stage of granulation tissue is that of indifference, the next that of the myxomatous type. The tissue filling a wound and that filling the burst Graafian follicle are identical.

With the knowledge obtained from the study of an early human corpus luteum, I will proceed to the analysis of the corpora

lutea of animals, those of the sow, the ewe, and the cow. Fig. 4 represents such corpora lutea in cross-sections of the ovaries in natural size.

*B. Corpus Luteum of the Sow.*—The fertility of this animal is well illustrated by the three corpora lutea almost filling the substance of the ovary; what is left of the ovarian tissue is conspicuous by a number of cavities representing the so-called small cystic degeneration of the ovary. I here wish to state that all the cavities that honeycomb the ovary of the sow are Graafian follicles in different stages of development.

With low powers of the microscope we can ascertain that each corpus luteum is surrounded by a capsule of fibrous connective tissue, which at the most peripheral portions is identical with the capsule of the ovary itself. The capsule is freely supplied with arteries, veins, and capillaries. The latter varieties of ves-

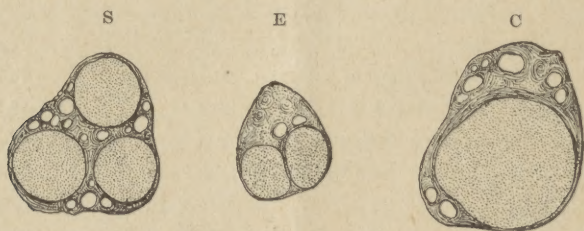


FIG. 4.—Cross-sections of ovaries with corpora lutea of pregnancy, natural size. S, ovary of sow; E, ovary of ewe; C, ovary of cow.

sels are often seen widened and taking a concentric course around the corpus luteum. The fibrous connective tissue sends scanty offshoots into the depth of the corpus luteum, accompanying the arteries and veins, but nowhere producing regular septa as in the human ovary. In fact, the blood supply of the corpus luteum of the sow is but scanty.

With medium powers of the microscope the corpus luteum of the sow yields the striking appearance presented in Fig. 5.

I have selected for illustration a portion traversed by an arteriole, which is accompanied by a delicate layer of fibrous connective tissue sending minute offshoots between the large protoplasmic bodies. The vein visible in the same field has only a narrow adventitial coat of fibrous connective tissue, but no muscle fibres in its wall. The most striking features are the bluntly polyhedral, protoplasmic bodies scattered almost uniformly throughout the corpus luteum. These bodies are con-

spicuous by a yellowish-brown color and the lack of ammoniacal carmine stain; they are coarsely granular, distinctly nucleated; the majority are pale, and only here and there we meet with dark-brown bodies. Not infrequently the body appears retracted from the adjacent connective-tissue sheath, whereby a light gap is produced. Occasionally such a body contains vacuoles, or the body may have dropped out from its sheath and left a light gap. Each corpuscle is surrounded by a delicate layer of fibrous connective tissue which has taken the carmine stain. This stain is



FIG. 5.—Fully developed corpus luteum of sow.  $\times 500$ . A, artery; V, vein, with partly detached endothelia; E, E, endothelia filling the meshes of the fibrous connective tissue; N, vacuolated endothelium; F, F, fibrous connective tissue between the endothelia; H, empty space, the endothelium dropped out; M, endothelium composed of medullary corpuscles.

especially pronounced in the protoplasmic formations lying in the broadest portions of the sheath, the so-called connective-tissue corpuscles.

What are the protoplasmic bodies under consideration?

In order to settle this question we must resort to the highest powers of the microscope (see Fig. 6).

We are struck by the reticulated structure, which is seen in the nuclei as well as in the surrounding protoplasm. The

nuclei are coarsely granular and bordered by a distinct shell in the majority of the bodies. They are sometimes located in the centre of the body, sometimes eccentrically. In the dark-brown bodies the nuclei are not globular, but irregularly shaped, often exhibiting indistinct karyokinetic figures (D D). The granules vary in size in the pale bodies, but are more uniform in size in the brown ones. All granules, it is immaterial whether in the nucleus or in the surrounding protoplasm, are united with one another by delicate, thorny offshoots. The stain so characteris-

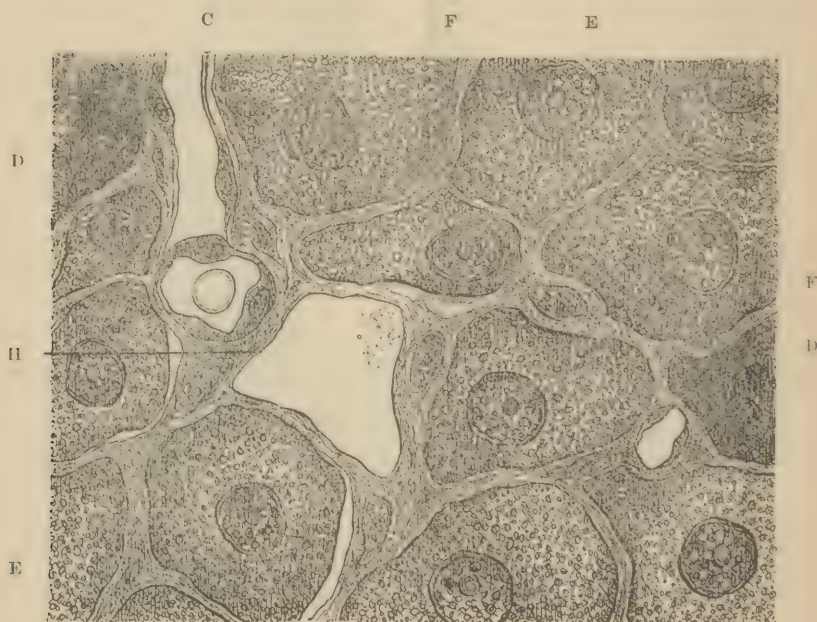


FIG. 6.—Fully developed corpus luteum of sow.  $\times 1200$ . E, E, non-pigmented endothelia; D, D, pigmented endothelia; F, F, frame of delicate fibrous connective tissue; H, space left after dropping out of endothelium; C, capillary blood vessel.

tic of the bodies under consideration is always diffuse, uniformly distributed in the granules of the protoplasm both in the pale and the dark bodies. The nuclei of the surrounding connective tissue are likewise granular, but differ from the large bodies by their carmine stain.

From what we have learned in the human corpus luteum we are justified in asserting, firstly, that each large body is the outcome of coalescence of a number of indifferent or medullary corpuscles; indications of such a splitting up are recognizable in

Fig. 5, M. Secondly, we must term the large bodies endothelia, and not epithelial or epithelioid cells, since they are the offspring of indifferent corpuscles, all together of the type of connective-tissue formations. Thirdly, we admit that the brownish color of these endothelia is due to the hemoglobin dissolved out of the red blood corpuscles that have first filled the cavity left by the rupture of the Graafian follicle. The term lutein cells is applicable to the endothelia of the corpus luteum, although it has no proper sense.

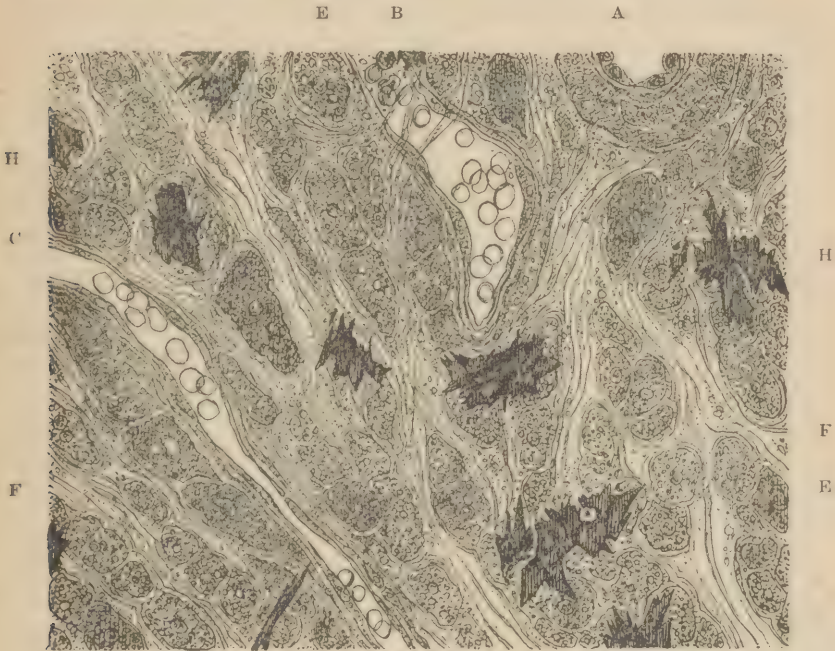


FIG. 7.—Corpus luteum of sow in involution.  $\times 400$ . E, E, endothelia, partly coarsely and partly finely granular, all slightly pigmented; F, F, interstitial delicate fibrous connective tissue; H, H, hematoidin crystals; A, artery, the middle coat broken up to medullary corpuscles; C, capillary blood vessel; B, red blood corpuscles within a capillary, in beginning change to hematoidin.

In the history of development of the myxomatous tissue, more especially of the umbilical cord and the granuloma of healing wounds, we invariably notice the origin from indifferent corpuscles which have been infiltrated with a myxomatous basis substance. A number of such bodies are surrounded by unchanged protoplasmic bodies, branching and interconnecting, or by a network of delicate fibrous connective tissue which at the

points of intersection still retains a nucleus. If we say that the corpus luteum is composed of myxomatous tissue in which no infiltration with basis substance has taken place, but the protoplasmic condition has been retained indefinitely, I believe we have a proper definition of the tissue building up the corpus luteum.

The corpus luteum is a transient formation which attains full development during gestation and disappears after delivery. It is of considerable interest to trace the changes that are characteristic of the involution of the corpus luteum (see Fig. 7).

Whereas the latter is easily discernible with the naked eye, there is scarcely a possibility of recognizing a corpus luteum in involution except on account of a slight brownish discoloration. Under the microscope the most prominent feature is an abundance of rust-brown hematoidin crystals scattered both throughout the corpus luteum and the connective tissue in the immediate vicinity. The pigmented, coarsely granular endothelia are still present, though much less in number and much smaller in size than in the corpus luteum at the full height of its development. The fibrous connective tissue, on the contrary, is far more abundant. There is but one possibility of explaining this change, and this is, a return of the endothelia into the embryonal state by breaking up into medullary or indifferent corpuscles, which split up into spindles and become fibrous connective tissue after infiltration with glue-yielding basis substance.

This assumption is justified by the study of the corpus luteum in involution. Each cluster of coarsely granular, diffusely pigmented bodies proves to be a remnant of a previous endothelium. At the same time a paling of the protoplasm has taken place, due to a decrease in the number of granules within the medullary corpuscles. Thus an originally coarsely granular and pigmented body is changed into a finely granular, non-pigmented one. Not only will this change facilitate the transformation into fibrous connective tissue, but also the absorption through the lymphatics, as the study of the senile changes of the connective tissue proves.

I wish to draw attention to the red blood corpuscles within a capillary blood vessel, depicted in Fig. 7, B. Here a few red blood corpuscles have taken up a dark yellow-brown color, and in them have appeared small, prismatic crystals of hematoidin. This occurrence explains one source of the hematoidin. An-

other source was found in the involuted corpus luteum in small hemorrhages scattered in the connective tissue. The extravasated blood certainly can assist in the production of hematoidin crystals. By a coalescence of prisms originate the peculiarly shaped rust-brown clusters of hematoidin so characteristic of the process of involution of the corpus luteum.

*C. Corpus Luteum of the Ewe.*—The naked-eye appearance (Fig. 4, E) is not essentially different from that of a sow's ovary, since here, too, we notice the brownish color, delicate rents due

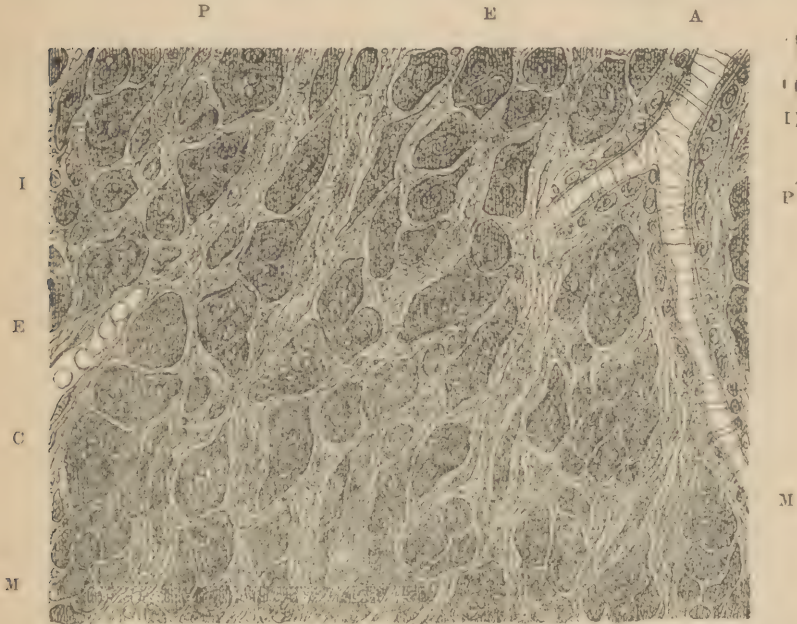


FIG. 8.—Fully developed corpus luteum of ewe.  $\times 400$ . E, E, coarsely granular, diffusely pigmented endothelia; M, M, clusters of medullary corpuscles; I, I, interstitial connective tissue; P, P, protoplasmic bodies, partly pigmented, in the interstitial tissue; A, artery; C, capillary blood vessel.

to blood vessels, but no lobulation whatever. With low powers of the microscope we can ascertain the fact that toward the periphery each corpus luteum is covered only by a thin connective-tissue capsule blending with that of the ovary itself. In one specimen I have seen a shallow depression on the surface of the ovary, corresponding to a slightly thickened knot of connective tissue, still crowded with protoplasmic bodies, from which the elongated endothelia and the blood vessels took a radiating

course. Obviously this knot was the healed wound produced by the rupture of the Graafian follicle. The vascular supply of the capsule of the corpus luteum is more abundant than in the sow, though it must be conceded that the ewe's ovary contains far more blood vessels in its substance than that of the sow. Especially are the arteries and arterioles of the ewe's ovary conspicuous by beautifully developed smooth muscle fibres. With a power of about four hundred diameters the corpus luteum of the ewe has the following appearance (Fig. 8):

The endothelia are of a pronounced yellow-brown tint; they are much smaller than those of the sow; they often exhibit two or more nuclei, and are frequently found to be composed of medullary or embryonal corpuscles. Even single endothelia vary greatly in size and shape; often they are found elongated, particularly so at the spot of the previous rupture of the follicle. The amount of fibrous connective tissue is far greater than in the sow, and this tissue carries a number of protoplasmic bodies, many of which are elongated and spindle-shaped, not admitting a thorough diagnosis, whether we have to place them among the endothelia or the connective-tissue corpuscles, since they often exhibit a yellow-brown pigmentation.

Of my specimens, four were obtained from pregnant ewes of about two months' term, and four from ewes some time after delivery.

I can say that the total appearance of the tissue is more juvenile than in the sow, and corresponds to an earlier stage of development of the sow's corpus luteum. The vascular supply of the ewe's corpus luteum is somewhat richer than that of the sow.

With high powers we ascertain all features described in the sow's corpus luteum, as to the structure of the large protoplasmic bodies and their nuclei. The latter, however, often appear as solid lumps or clusters of large, homogeneous, glossy granules. The process of involution of a corpus luteum of a previous pregnancy is similar to that of the sow (Fig. 9).

I have selected a low power for the representation of a corpus luteum, mainly to illustrate the fact that one portion may be crowded with hematoidin crystals, another entirely destitute of them. The crystals, therefore, are not an essential feature of the retrogressive metamorphosis of a corpus luteum. One of the sources of such crystals seems to be the pigmented

endothelia themselves (H), since I have seen small rust-brown prisms embedded in single endothelia. The latter, though still coarsely granular, are on an average smaller than those of the fully developed corpus luteum, and their hue is paler. Obviously a reduction of many coarsely granular bodies has taken place into finely granular and non-pigmented bodies, with a final change into fibrous connective tissue. Small, finely granular bodies are seen embedded in large numbers within the fibrous tissue, not differing materially from ordinary connective-

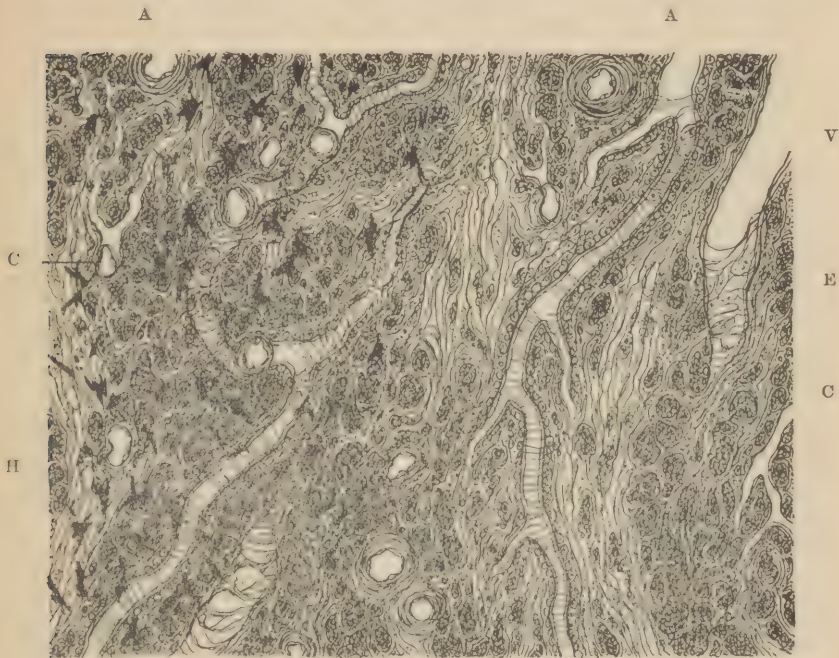


FIG. 9.—Corpus luteum of ewe in involution.  $\times 200$ . H, portion of corpus luteum richly supplied with hematoidin crystals; E, portion of corpus luteum destitute of hematoidin crystals; A, A, arteries; V, vein; C, C, capillaries.

tissue corpuscles. They are recognizable by a slight yellow-brown tint as previous endothelia, only they are more crowded.

The delicate fibrous tissue is freely supplied with arterioles, veins, and capillaries, all of a more or less tortuous course, obviously due to the shrinkage of the bulk of the corpus luteum. Some of the veins are partly filled with a myxomatous tissue, due to a proliferation of the endothelia, and finally leading to the obliteration of the vessel. A similar process is noticeable

in many capillary blood vessels that have been transformed into fibrous connective tissue. The arterioles, on the contrary, have not undergone changes in their constituent elements. The study of the vicinity of the shrivelled corpus luteum enables me to state that the final result of the involution is cicatricial, fibrous connective tissue.

*D. Corpus Luteum of Cow.*—With the naked eye we see (Fig. 4, C) a globular formation, indistinctly lobulated, of a considerable size. It is surrounded by a concentrically striated cap-

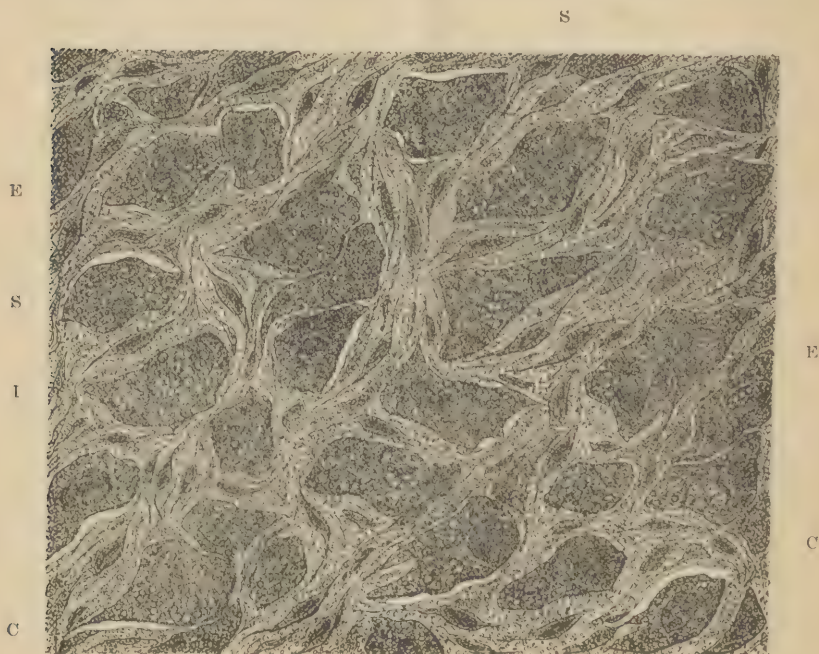


FIG. 10.—Fully developed corpus luteum of cow.  $\times 400$ . E, E, coarsely granular, diffusely pigmented endothelia; I, I, interstitial connective tissue; S, S, spindle-shaped protoplasmic bodies; C, C, coarsely granular protoplasmic bodies slightly pigmented.

sule, blending at the most peripheral portion with the capsule of the ovary. The rest of the ovary is pierced by cavities of varying size, which by closer analysis prove to be follicles in different stages of development.

Low powers show that the corpus luteum is traversed by fibrous septa running irregularly and carrying the blood vessels of the three types. The vascular supply of the main mass is but scanty, that of the capsule, on the contrary, abundant. Only

the tissue of the capsule and the septa emanating therefrom have taken the carmine stain, while the main mass lacks this stain and exhibits a yellow-brown color, nowhere of a deep tint. The main mass is composed of polyhedral, large-sized endothelia and a considerable amount of ensheathing fibrous tissue. The size of the endothelia is largest at the most peripheral portion, nearest to the previous rupture, where they appear much elongated and take a radiating course toward the rupture. In the latter situation the capillaries are most numerous and conspicuous by their straight course. The appearance of the main mass is represented in Fig. 10.

We are struck at once by the large size and angular shape of the endothelia. Many of these have long, pointed offshoots, rendering them pear-shaped or triangular. Interspersed among the large endothelia we occasionally observe small ones, likewise of angular contours. The granulation in the protoplasm is apparent by its coarseness and variance in size. The nuclei are but indistinctly defined, also composed of coarse granules densely packed together. In some bodies two and more nuclei are traceable, in others none, either being really absent or merely concealed by the coarse granules of the protoplasm. The pigmentation is diffusely distributed throughout the granules of both protoplasm and nuclei.

The fibrous connective tissue which ensheathes the endothelia is conspicuous by its abundance and the large number of spindle-shaped protoplasmic bodies or connective-tissue corpuscles. The fibrillation of this tissue is nowhere pronounced. The large amount of interstitial tissue, as compared with the corpora lutea of the sow and the ewe, and the variety of the size of the endothelia, indicate that the corpus luteum under consideration has really passed its full height of development and has begun to enter retrograde changes. This coincides with the fact that the cow is usually slaughtered four to five months after delivery. We can justly assume, therefore, that the corpus luteum which we are studying is one in thirteen or fourteen months of its existence.

The process of involution is sometimes marked by an abundance of hematoidin—so much so that such a corpus luteum is recognizable to the naked eye by its rust-brown color. But I have met with corpora lutea in involution lacking hematoidin crystals altogether, so that I would reiterate my remark, made

in the description of the ewe's ovary, that hematoidin is not an essential feature in the process of involution of a corpus luteum. The ordinary appearance of this formation is illustrated in Fig. 11.

The breaking up of the original endothelia into medullary or embryonal corpuscles is at once noticeable. The granules at the same time have become scantier and apparently less pigmented. The pigmentation has different degrees. Some medullary corpuscles are still yellow-brown, though comparatively



FIG. 11.—Corpus luteum of cow in involution.  $\times 400$ . M, M, bundle of smooth muscle fibres; L, L, coarsely granular, pigmented endothelia (so-called lutein cells); P, P, almost pigmentless endothelia, with scattered granules; B, coarsely granular endothelium, showing the beginning formation of hematoidin; F, F, faintly striated interstitial connective tissue; H, H, crytals of hematoidin; C, C, capillary blood vessels.

few in number; in others the paling has attained such a degree that they do not differ from ordinary protoplasm; whereas some appear but finely granular, indistinctly nucleated, as if in the process of infiltration with basis substance. Here and there we meet with small fields of a myxomatous connective tissue, which fields may have taken origin from the obliteration of capillary and venous blood vessels.

The clusters of hematoidin crystals are large and many-shaped. Again I have been able to trace their origin from the coloring matter of coarsely granular medullary corpuscles (B), in which the granules assume a dark red-brown color before giving rise to hematoidin prisms. Such images are also seen at L, and further toward the lower centre of the figure.

In the illustrated portion a bundle of smooth muscle fibres is seen traversing the tissue of the corpus luteum (M, M). I have no right to maintain that the muscle fibres are newly formed,

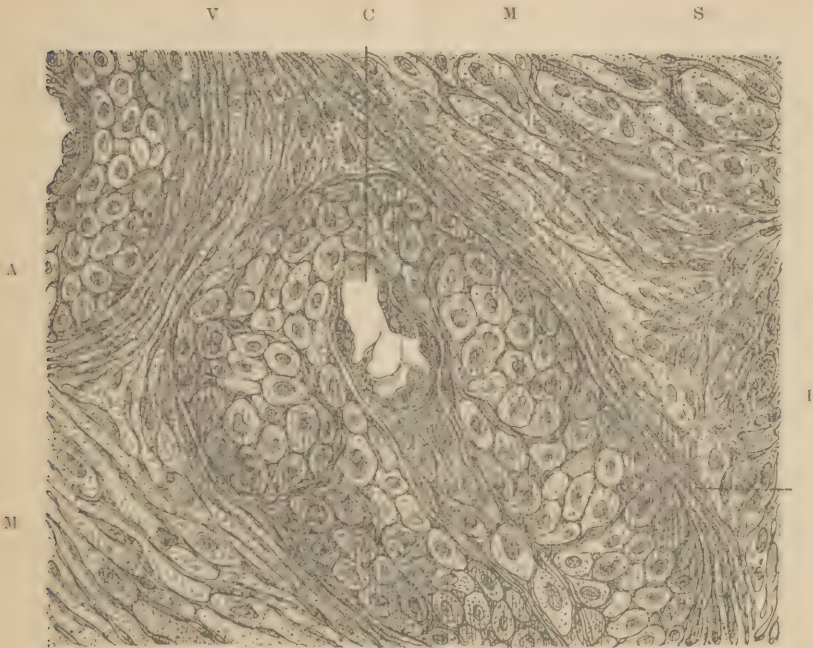


FIG. 12.—Tissue changes around a cow's corpus luteum in involution.  $\times 400$ . A, artery in transverse section, the muscle coat transformed into myxomatous tissue; C, calibre of an artery in oblique section, the endothelia in proliferation; V, V, adventitial coat of the artery; M, M, myxofibrous connective tissue; I, medullary tissue; S, remnants of smooth muscle fibres.

the less since they likewise contain clusters of hematoidin crystals. This feature renders it probable that we have a bundle of smooth muscle fibres before us which originally traversed the cortex of the ovary in the vicinity of the Graafian follicle, and has escaped changes in the process of new formation following the rupture.

Lastly, I wish to draw attention to the tissue changes that

take place in the immediate vicinity of a corpus luteum in involution (Fig. 12).

The arteries are here conspicuous by their narrow calibre and the bulk of the middle coat. Obviously this coat has changed its original structure of smooth muscle fibres into a delicate myxomatous tissue, as best illustrated in the cross-section of an artery (A), where the radiating fibres of the smooth muscle ought to be seen. In Fig. 7, A, I have drawn a cross-section of an artery in an involuted corpus luteum of the sow, where the smooth muscles are broken up into small medullary corpuscles. From this embryonal tissue evidently develops the myxomatous tissue forming the middle coat of the artery in Fig. 12. The artery C shows a beginning proliferation of the endothelia lining its calibre, the result of which is the appearance of a first embryonal, afterward myxomatous tissue, which obliterates the calibre to complete impermeability. A similar change takes place in many veins, as mentioned before, yielding a myxomatous tissue in place of obliterated veins. Both the adventitial coat of the arteries and the tissue bordering on the disappearing corpus luteum are of a tissue variety best defined as myxofibrous, since in the meshes of the network of the delicate fibres myxomatous basis substance is deposited. The residues of smooth muscle fibres are likewise embedded in, and surrounded by, a myxomatous and myxofibrous reticulum.

These latter varieties of tissue, together with newly formed fibrous connective tissue, establish the comparatively small cicatrix, the last outcome of a previous corpus luteum of pregnancy.

The results of my comparative studies of the corpus luteum I would sum up in the following paragraphs:

1. The corpus luteum is a new formation of tissue, filling the loss of substance after the rupture of a Graafian follicle and fructification of the ovum.
2. In its production not only the wall of the ruptured follicle, but also the tissue of the ovary next to the follicle, and probably the remnants of the follicular epithelium, participate; thus the corpus luteum is considerably larger than the space occupied by the original follicle.
3. The corpus luteum is, in its earliest stages of development, of an embryonal or medullary or indifferent tissue, similar to that of the embryo in the first weeks of its growth.
4. The medullary tissue is the outcome of changes identical

with those termed inflammatory. Fibrous connective tissue, smooth muscle fibres, and blood vessels break up by proliferation of their living matter, both of the protoplasm and basis substance, into indifferent corpuscles, united among themselves, representing the embryonal tissue.

5. The human corpus luteum of the second month of pregnancy is composed of a lobulated, cortical portion of embryonal and a central portion of myxomatous tissue. The corpora lutea of the sow, the ewe, and the cow are non-lobular and uniform in structure throughout.

6. The medullary elements, originally arranged in groups, produce by coalescence large, nucleated, protoplasmic bodies, the lutein or epithelioid cells of authors. They are pigmented by the hemoglobin of the extravasated blood corpuscles first filling the cavity of the ruptured follicle.

7. The large, coarsely granular, protoplasmic bodies should be termed "endothelia," and the tissue building up the corpus luteum "endothelioma"—*i.e.*, myxomatous tissue, in which the protoplasmic bodies persist instead of being infiltrated with basis substance.

8. The tissue of the corpus luteum is similar to that of a granuloma. The former is the result of a physiological, the latter a pathological reparative process. Both are myxomatous tissue.

9. In the corpus luteum the meshes of the myxomatous tissue remain throughout its persistence protoplasmic in the shape of coarsely granular, nucleated bodies, the endothelia. In the granuloma the meshes are soon infiltrated with myxomatous basis substance.

10. In the process of involution of the corpus luteum the endothelia break up into medullary corpuscles, which build up fibrous connective tissue. This process is often, but not invariably, accompanied by the appearance of clusters of hematoidin crystals.

11. The hematoidin crystals have a threefold source: red blood corpuscles contained in partly obliterated blood vessels; small extravasations of blood in the retrogressive changes of the venous and capillary blood vessels of the corpus luteum; and, lastly, the endothelia themselves, saturated with hemoglobin from their very origin.

12. The final result of the involution of the corpus luteum is cicatricial tissue, built up first by myxomatous, later myxofibrous, and at last by fibrous connective tissue.







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